Attorney Docket No.: AVZ-001CPUSCN2

Examiner: J. Lundgren Group Art Unit: 1639

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

- 1. (Currently Amended) A method for treating a subject afflicted with a nervous system disease comprising administering to the subject an amount of creatine, creatine phosphate or a creatine analog or a salt thereof empound sufficient to prevent, reduce, ameliorate or eliminate said disease.
- 2. (Original) The method of claim 1 wherein the subject is a mammal.
- 3. (Original) The method of claim 1 wherein the subject is human.
- 4. (Original) A method for treating a subject for diseases of the nervous system comprising: administering an effective amount of a creatine compound to a subject such that the subject is treated for diseases of the nervous system, wherein the creatine compound is of the general formula:

$$Z_1$$
 $C = X - A - Y$

and pharmaceutically acceptable salts thereof, wherein:

- a) Y is selected from the group consisting of: $-CO_2H$, -NHOH, $-NO_2$, $-SO_3H$, $-C(=0)NHSO_2J$ and -P(=O)(OH)(OJ), wherein J is selected from the group consisting of: hydrogen, C_1 - C_6 straight chain alkyl, C_3 - C_6 branched alkyl, C_2 - C_6 alkenyl, C_3 - C_6 branched alkenyl, and aryl;
- b) A is selected from the group consisting of: C, CH, C₁-C₅alkyl, C₂-C₅alkenyl, C₂-C₅alkynyl, and C₁-C₅ alkoyl chain, each having 0-2 substituents which are selected independently from the group consisting of:
- 1) K, where K is selected from the group consisting of: C₁ -C₆ straight alkyl, C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl,

U.S.S.N. 10/718,765 Attorney Docket No.: AVZ-001CPUSCN2

C₃-C₆ branched alkenyl, and C₄-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

Examiner: J. Lundgren

Group Art Unit: 1639

- an aryl group selected from the group consisting of: a 1-2 ring carbocycle and a 1-2 ring heterocycle, wherein the aryl group contains 0-2 substituents independently selected from the group consisting of: -CH₂L and -COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy; and
- 3) -NH-M, wherein M is selected from the group consisting of: hydrogen, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₁-C₄ alkoyl, C₃-C₄ branched alkyl, C₃-C₄ branched alkenyl, and C₄ branched alkoyl;
- c) X is selected from the group consisting of NR₁, CHR₁, CR₁, O and S, wherein R₁ is selected from the group consisting of:
 - 1) hydrogen;
- 2) K where K is selected from the group consisting of: C₁-C₆ straight alkyl, C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, and C₄-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
- 3) an aryl group selected from the group consisting of a 1-2 ring carbocycle and a 1-2 ring heterocycle, wherein the aryl group contains 0-2 substituents independently selected from the group consisting of: -CH₂L and -COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
- 4) a C₅-C₉ a-amino-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon;
- 5) a C₅-C₉ a-amino-w-aza-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon; and
- 6) a C₅-C₉ a-amino-w-thia-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon;

U.S.S.N. 10/718,765 Examiner: J. Lundgren Attorney Docket No.: AVZ-001CPUSCN2 Group Art Unit: 1639

d) Z_1 and Z_2 are chosen independently from the group consisting of: =0, -NHR₂, -CH₂R₂, -NR₂OH; wherein Z_1 and Z_2 may not both be =0 and wherein R₂ is selected from the group consisting of:

1) hydrogen;

- 2) K, where K is selected from the group consisting of: C₁-C₆ straight alkyl; C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, and C₄-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
- an aryl group selected from the group consisting of a 1-2 ring carbocycle and a 1-2 ring heterocycle, wherein the aryl group contains 0-2 substituents independently selected from the group consisting of: -CH₂L and -COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
 - 4) a C₄-C₈ a-amino-carboxylic acid attached via the w-carbon;
- B, wherein B is selected from the group consisting of: $-CO_2H$, -NHOH, $-SO_3H$, $-NO_2$, OP(=O)(OH)(OJ) and -P(=O)(OH)(OJ), wherein J is selected from the group consisting of: hydrogen, C_1 - C_6 straight alkyl, C_3 - C_6 branched alkelyl, C_3 - C_6 branched alkelyl, and aryl, wherein B is optionally connected to the nitrogen via a linker selected from the group consisting of: C_1 - C_2 alkyl, C_2 alkelyl, and C_1 - C_2 alkoyl;
- of: C1-C3 straight alkyl, C3 branched alkyl, C2-C3 straight alkenyl, C3 branched alkenyl, C1-C3 straight alkoyl, aryl and aroyl; and E is selected from the group consisting of: -(P03)_nNMP, where n is 0-2 and NMP is ribonucleotide monophosphate connected via the 5'-phosphate, 3'-phosphate or the aromatic ring of the base; -[P(=O)(OCH3)(0)]_m-Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; -[P(=O)(OH)(CH2)]_m-Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; and an aryl group containing 0-3 substituents chosen independently from the group consisting of: Cl, Br, epoxy, acetoxy, -OG, -C(=O)G, and -CO2G, where G is independently selected from the group consisting

Examiner: J. Lundgren Group Art Unit: 1639

U.S.S.N. 10/718,765 Attorney Docket No.: AVZ-001CPUSCN2

of: C₁-C₆ straight alkyl, C₂-C₆ straight alkenyl, C₁ -C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, C₄-C₆ branched alkoyl, wherein E may be attached to any point to D, and if D is alkyl or alkenyl, D may be connected at either or both ends by an amide linkage; and

- -E, wherein E is selected from the group consisting of $(P0_3)_nNMP$, where n is 0-2 and NMP is a ribonucleotide monophosphate connected via the 5'-phosphate, 3'-phosphate or the aromatic ring of the base; - $[P(=O)(OCH_3)(0)]_m$ -Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; - $[P(=O)(OH)(CH_2)]_m$ -Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; and an aryl group containing 0-3 substituents chose independently from the group consisting of: C₁, Br, epoxy, acetoxy, -OG, -C(=O)G, and -CO=G, where G is independently selected from the group consisting of: C₁-C₆ straight alkyl, C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkenyl, C₄-C₆ branched alkoyl; and if E is aryl, E may be connected by an amide linkage;
- e) if R₁ and at least one R₂ group are present, R₁ may be connected by a single or double bond to an R₂ group to form a cycle of 5 to 7 members;
- f) if two R₂ groups are present, they may be connected by a single or a double bond to form a cycle of 4 to 7 members; and
- g) if R_1 is present and Z_1 or Z_2 is selected from the group consisting of NHR₂, -CH₂R₂ and -NR₂OH, then R_1 may be connected by a single or double bond to the carbon or nitrogen of either Z_1 or Z_2 to form a cycle of 4 to 7 members.
- 5. (Original) The method of claim 4 wherein the treatment comprises reducing or eliminating symptoms associated with a preexisting disease of the nervous system.
- 6. (Original) The method of claim 4 wherein the treatment comprises preventing the occurrence of diseases of the nervous system within the subject.
- 7. (Original) The method of claim 4 wherein the creatine compound is creatine.

U.S.S.N. 10/718,765 Examiner: J. Lundgren
Attorney Docket No.: AVZ-001CPUSCN2 Group Art Unit: 1639

8. (**Original**) The method of claim 4 wherein the creatine compound is creatine phosphate.

- 9. (Withdrawn) The method of claim 4 wherein the creatine compound is cyclocreatine.
- 10. (Withdrawn) The method of claim 4 wherein the creatine compound is cyclocreatine phosphate.
- 11. (Withdrawn) The method of claim 4 wherein the creatine compound is homocyclocreatine.
- 12. (**Original**) The method of claim 4 wherein the disease of the nervous system is selected from the groups consisting of neuropathies; Alzheimer disease, Parkinson's disease, Huntington's disease, motor neuron disease, traumatic nerve injury, multiple sclerosis, acute disseminated encephalomyelitis, acute necrotizing hemorrhagic leukoencephalitis, dysmyelination disease, mitochondrial disease, migrainous disorder, bacterial infection, fungal infection, stroke, aging, dementia, peripheral nervous system diseases and mental disorders such as depression and schizophrenia.
- 13. (**Original**) The method of claim 12 wherein the creatine compound is selected from the group consisting of creatine, creatine phosphate, cyclocreatine and cyclocreatine phosphate.
- 14. (**Original**) The method of claim 4 further comprising coadministering to the subject a neurotransmitter, a neurotransmitter analog, a steroid, an immunomodulating agent, or an immune suppressive agent.
- 15. (**Original**) The method of claim 4 wherein the subject is treated for diseases of the nervous system by reducing or eliminating symptoms associated with a preexisting diseases of the nervous system.
- 16. (**Original**) The method of claim 4 wherein the subject is treated for diseases of the nervous system by preventing the occurrence of a disease of the nervous system within the subject.

U.S.S.N. 10/718,765 Examiner: J. Lundgren
Attorney Docket No.: AVZ-001CPUSCN2 Group Art Unit: 1639

17. (**Original**) A method for alleviating in a subject being treated for a nervous system disease toxic side effects of drugs used to treat the nervous system diseases, comprising administering to the subject an amount of a creatine, creatine phosphate or a creatine analog, or a salt thereof, sufficient to prevent, reduce, ameliorate or alleviate said toxic side effects.

- 18. (Withdrawn) The method of claim 17 wherein the creatine analog is cyclocreatine or cyclocreatine phosphate.
- 19. (New) A method for treating a subject with Huntington's disease, comprising administering to the subject an effective amount of creatine, creatine phosphate or a creatine analog or a salt thereof sufficient to reduce, ameliorate or eliminate Huntington's disease.
- 20. (New) The method of claim 19, wherein said subject is administered an effective amount of creatine.
- 21. (New) The method of claim 19, wherein said subject is administered an effective amount of creatine phophate.
- 22. (New) The method of claim 19, further comprising coadministering to the subject a neurotransmitter, a neurotransmitter analog, an immunomodulating agent, or an immune suppressive agent.
- 23. (New) The method of claim 19, further comprising coadministering to the subject a a steroid.